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# Computational simulation of intracoronary flow based on real coronary geometry☆,☆☆,☆☆☆

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**Abstract**

**Objective**: To assess the feasibility of computationally simulating intracoronary blood flow based on real coronary artery geometry and to graphically depict various mechanical characteristics of this flow. **Methods**: Explanted fresh pig hearts were fixed using a continuous perfusion of 4% formaldehyde at physiological pressures. Omnipaque dye added to lead rubber solution was titrated to an optimum proportion of 1:25, to cast the coronary arterial tree. The heart was stabilized in a phantom model so as to suspend the base and the apex without causing external deformation. High resolution computerized tomography scans of this model were utilized to reconstruct the three-dimensional coronary artery geometry, which in turn was used to generate several volumetric tetrahedral meshes of sufficient density needed for numerical accuracy. The transient equations of momentum and mass conservation were numerically solved by employing methods of computational fluid dynamics under realistic pulsatile inflow boundary conditions. **Results**: The simulations have yielded graphic distributions of intracoronary flow stream lines, static pressure drop, wall shear stress, bifurcation mass flow ratios and velocity profiles. The variability of these quantities within the cardiac cycle has been investigated at a temporal resolution of 1/100th of a second and a spatial resolution of about 10 μm. The areas of amplified variations in wall shear stress, mostly evident in the neighborhoods of arterial branching, seem to correlate well with clinically observed increased atherogenesis. The intracoronary flow lines showed stasis and extreme vorticity during the phase of minimum coronary flow in contrast to streamlined undisturbed flow during the phase of maximum flow. **Conclusions**: Computational tools of this kind along with a state-of-the-art multislice computerized tomography or magnetic resonance-based non-invasive coronary imaging, could enable realistic, repetitive, non-invasive and multidimensional quantifications of the effects of stenosis on distal hemodynamics, and thus help in precise surgical/interventional planning. It could also add insights into coronary and bypass graft atherogenesis.


*Keywords:* Atherogenesis; Coronary flow; Computational flow simulation; Non-invasive coronary imaging; Surgical planning

## 1. Introduction

The use of principles of mechanics to predict flow in vascular systems is not new. A great amount of scientific effort has already been invested on calculating the mechanical characteristics of physiological and pathological arterial blood flow [1–3]. Intracoronary flow has been simulated with several degrees of approximation by various researchers. Conventional one-dimensional steady hemodynamic analyses have been performed on several anatomically accurate models of the porcine coronary vasculature [4,5]. Unsteady solutions of a similar simplified set of equations that take into account the elasticity of the arterial

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walls have also been presented [6]. Complete three-dimensional (3D) analyses of the mechanical characteristics of coronary flow have so far been constrained to idealized tube like geometries [7,8] or more recently to isolated, segments of the real coronary anatomy without branches [9–12]. The use of high speed computational techniques is rapidly changing the potential to which such techniques could help in the diagnosis, management and even prediction of vascular diseases. Herein this study we try to assess the feasibility of recreating pulsatile blood flow in an anatomically accurate porcine coronary vasculature by using high speed computational techniques.

Computational fluid dynamics (CFD) techniques are capable of allowing realistic simulation of vascular hemodynamics of patients in a completely virtual environment. An 'a priori', objective, multidimensional quantification of the flow distal to a coronary stenosis for example, would greatly assist the diagnosis and management of coronary artery diseases. In the era of minimally invasive surgical approaches, where the surgeon has to adapt to increasing restriction of use of native visual and tactile senses, CFD could assist preoperative surgical planning.

It has been reported that mechanical properties of blood flow such as spatial and temporal distributions of wall shear stress may contribute to atherogenesis and its proliferation [13]. CFD simulations may prove to be useful in investigating the role of hemodynamic stresses in atherogenesis. The purpose of this study is to investigate the feasibility of creating a realistic computational model, which could be used in clinical practice to provide objective information about the hemodynamic effects of vascular disease in the coronaries as well as guide the preplanning of the best revascularization strategy. Furthermore, we envision future uses of the developed methodology in interrogating the pathogenesis of atherosclerosis and its connection with hemodynamics.

## 2. Materials and methods

Since in vivo acquisition of a 3D anatomy of patient-specific coronary arterial tree remains technically very challenging mainly because of the cardiac motion, this study involved 3D modeling of the coronary vasculature of an explanted porcine heart. However, all techniques and tools developed could be readily used on in vivo human coronary tree acquisitions, as soon as they become routinely available.

### *2.1. Acquisition of 3D coronary geometry*

Several fresh explanted porcine hearts were perfused with a suitable solution of formaldehyde, omnipaque dye and lead rubber at physiological pressures so as to produce uniformly solidified 3D casts. Titrating omnipaque dye (1:25 proportion) in lead rubber solution was found to be

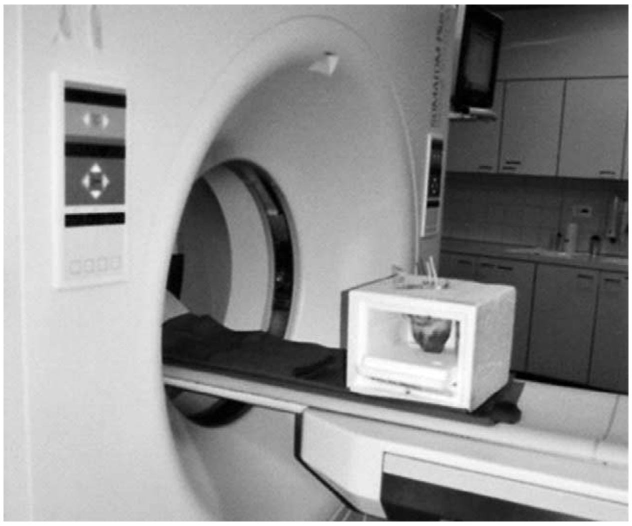

Fig. 1. Acquisition of porcine coronary anatomy.

optimum in avoiding excessive opacification, the so-called 'noise' during CT scanning. A thermocol model suspending the heart at the ascending aorta and stabilizing the apex in a slanted hole below was constructed to ensure stability during scanning and to prevent any artificially caused deformations. A 4-row detector Somatom Volume-Zoom (Siemens Medical Solution, Erlangen, Germany) CT-scanner was used to perform 1.25 mm thick slices of the porcine heart as shown in Fig. 1. The scanning parameters used for image acquisition included: detector collimation, $4 \times 1$ mm; slice thickness, 1.25 mm; pitch, 5; rotation time, 0.5 s; KVp, 180; mAs, 400. The high mAs value was required to reduce artifacts and background noise. The segmentation of the coronary arteries from the CT slices was achieved semi-automatically in a bi-step manner using commercially available specialized software, 'AMIRA 2.3' (Konrad Zuse Zentrum and Indeed Visual Concepts GmbH, Berlin, Germany).

In the first step, the software automatically segmented all the major branches based on light intensity threshold settings. Secondly, registering minor vessel branches as well as the addition of appropriate boundary endings was performed manually. The generation of an initial surface triangular mesh representing the inner arterial wall was constructed by the same software tool by utilizing a 'general marching cube' algorithm. To evaluate the segmentation procedure, the reconstructed coronary arterial walls were overlaid on the object-specific CT-slices for direct visual inspection (Fig. 2). Multiplanar reformation allowed comparison in axial, coronal and sagittal views.

### *2.2. Computational simulation: main assumptions and boundary conditions*

To begin with, this study focused on simulating flow in the left main coronary artery (LCA) and its main branches. The transient, incompressible, 3D equations of momentum

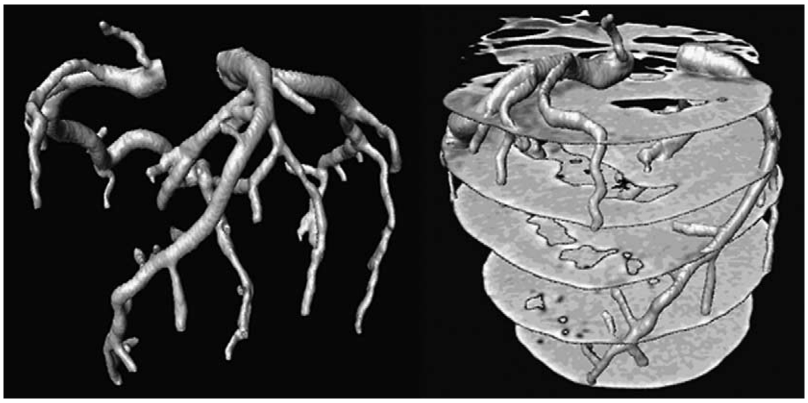

Fig. 2. Three-dimensional reconstructions of the coronary arteries.

and mass conservation were numerically solved. The incompressibility of the flowing medium is a plausible argument due to the liquid nature of blood and the relatively low velocity magnitudes that are developing throughout the human systemic and pulmonary circulations. The rheology of human blood was assumed to be Newtonian with a constant density of 1060 kg/m$^3$ at 37 °C and a constant dynamic viscosity of 0.0035 Pa s. The viscosity of blood is essentially constant at high shear rates (100 s$^{-1}$ in average), provided that the vessels' diameters exceed 1 mm and that the hematocrit retains a physiological value [14]. Non-Newtonian flow effects dominate blood flow in much smaller vessels with diameters less than 300 μm. In the present case the computational domain was sufficiently truncated by removing all arterial branches that possessed a diameter less than 1 mm for the sake of simplicity.

A periodical pulsatile volume inflow profile was applied as a velocity inlet boundary condition. These data refer to the average physiological human coronary flow and has been widely cited in the medical literature [15]. Based on this generic data, the average blood inflow into the LCA was calculated to be 57 ml/min reaching a maximum value of 105 ml/min during the diastolic phase.

The general equations of hemodynamics, as expressed by the momentum conservation equations, represent the balance of several kinds of forces [16]. In this case, the forces that are exerted upon any fluid element of the flow field may be distinguished into transient inertial forces, convective inertial forces, pressure and viscous forces. Several dimensionless parameters are used in fluid dynamics in order to characterize the relative strength of those forces and depend on the underlying geometry and boundary conditions. The Reynolds and the Womersley numbers are the main parameters that characterize the flow under investigation. They are defined below:

$$Re = \frac{U \cdot D \cdot \rho}{\mu} \qquad \text{and} \qquad a = \frac{D}{2}\left(\sqrt{\frac{\omega \cdot \rho}{\mu}}\right)$$

where $U$ denotes the average inflow velocity, $D$ is the vessel's diameter, $\rho$ is the density of blood, $\mu$ is the dynamic viscosity of blood and $\omega$ is the circular frequency of the pulsation. The Reynolds number, which characterizes the ratio of the convective inertial forces of the fluid to the viscous forces, has an average value of $Re = 108$ for the inflow conditions that were described above. Furthermore, it has a peak value slightly lower than $Re = 200$ for the coronary inlet diameter of approximately 3.4 mm. Under these conditions, the character of the flow can be safely presumed to be laminar. In the case of stenotic coronary arteries, the local Reynolds number may be significantly increased, thus warranting the use of an additional solver validated for transitional flows. The corresponding Womersley number, which is the ratio of the transient inertial forces (due to the imposed unsteady oscillatory inflow) to the viscous forces, is calculated to be $\alpha = 2.7$. This value corresponds to a cardiac cycle of 0.75 s or 80 bpm, which is the period of the assumed physiological pulsatile inflow profile. A large value for this parameter implies that the effect of the viscous forces does not propagate far from the walls but remains confined to an attached boundary layer. This is the case for the larger arteries of the human body like the aorta where the Womersley number is O(20) and the inertial forces dominate. In the coronaries this parameter has a small value implying that the exerted inertial forces are comparable to the viscous forces.

The spatial velocity profile at the inlet boundary surface, which stems directly from the aorta, was assumed to be uniform. This approximation is expected to be sufficiently accurate, considering that the LCA takes off at right angles to the orientation of the mean aortic blood flow and also because of the fact that its diameter is about one-10th to that of ascending aorta.

Furthermore, a no-slip wall boundary condition was imposed on every arterial wall. Contrary to normal physiology, the influences of coronary motion were neglected, since no reliable information about the complex human coronary artery motion is available. Currently, efforts are being undertaken to obtain detailed in vivo motion information using biplanar angiograms [17]. Conventionally, zero static pressure outflow boundary conditions have been used at all artificial outlet sections.

The selection of the above-described boundary condition is based on two premises. The first is to form a mathematically well-posed problem, while the second is to abide by the actual physiology as closely as possible.

The numerical solution of the discretized set of flow equations was performed by a finite volume, pressure correction Navier Stokes Solver 'CFD-ACE + ' (CFD Research Corporation, Huntsville, AL, USA), which utilizes 2nd order spatial and temporal discretization and multigrid acceleration. Implementation of case-specific boundary conditions was achieved by additional external user subroutines that are coupled to the main solver. A time resolution of 100 time steps per cardiac cycle was proven to be numerically sufficient.

### 2.3. Volumetric mesh generation

The complexity in the anatomy of the coronary arterial wall and lumen makes their geometrical description possible only through unstructured meshes. The 3D luminal volume was discretized into a multitude of analytical geometrical shapes called 'tetrahedra' (Fig. 3). This step was necessary to facilitate the discretization of the system of flow equations. Thus, a series of unstructured volumetric meshes were constructed by a grid generator 'GAMBIT 2.0.4' (Fluent Inc., Lebanon NH, USA). Special care was taken for the generation of meshes with high numerical quality, based on the initial representations of the inner arterial wall as derived by the segmentation procedure. The employed meshes contained 565 132, 711 665, 982 714 and 1 137 182 tetrahedra, respectively. A threshold value of 5% has been adopted for the maximum permissible change in the numerically calculated values of pressure and velocity within the flow domain. This criterion was shown to be satisfied between the last two of the constructed tetrahedral meshes. Hence, the last mesh containing a total number of 1 137 182 elements was affirmed to cover sufficiently the numerical requirements for stability and precision of the present investigation. It must be noted here that the computational costs, in terms of CPU power and memory consumption, increase exponentially with the total number of grid elements. The selected final grid constitutes a good compromise between computational tractability in terms of required time and accuracy.

The tetrahedral computational domain was truncated to maintain a minimum outflow cross-sectional diameter of 1 mm in accordance with the basic assumptions stated in Section 2.2. The various artificial domain boundaries, thus created, have been indicated as inlet or outlet sections and numbered suitably (Fig. 3). Blood flows through the inlet, into the computational domain and bifurcates continuously stepwise to the various arterial branches until it reaches one of the 12 artificial outlets.

## 3. Results

The computational simulations have produced detailed quantitative information on the hemodynamics of coronary flow under physiological pulsatile inflow conditions. These include instantaneous discharge blood flow ratios, wall shear stress and graphical depictions of intracoronary flow velocity profiles and streamlines.

### 3.1. Mass flow

A quantification of the blood flow rates through the two main branches of the LCA is shown in Fig. 4. The instantaneous history of blood flux through each of the outlets of our computational domain has also been plotted. These graphics allow us to determine the natural distribution of blood during pulsatile flow in the LCA system of this particular porcine heart. Once the newer imaging modalities start providing reliable coronary geometries including a 3D imaging of coronary stenosis, CFD techniques could define the extent of deficit in flow and the extent of drop in perfusion pressure distal to the stenosis.

The mass flow calculations in this study demonstrated that 71% of the total blood inflow is directed through the LAD and 29% through the LCX. This flow split ratio of 2.5 is largely maintained throughout the entire cardiac cycle thus indicating the absence of any significant stenosis or any

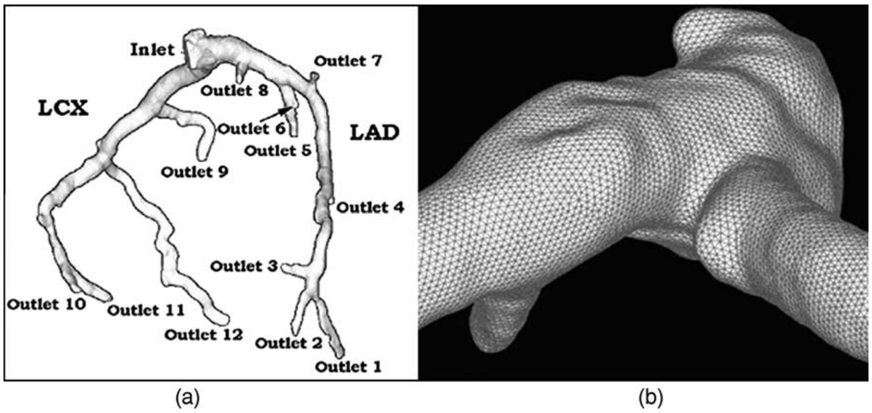


Fig. 3. (a) 3D view of the computational domain of porcine LCA. (b) Tetrahedral discretization of luminal volume.

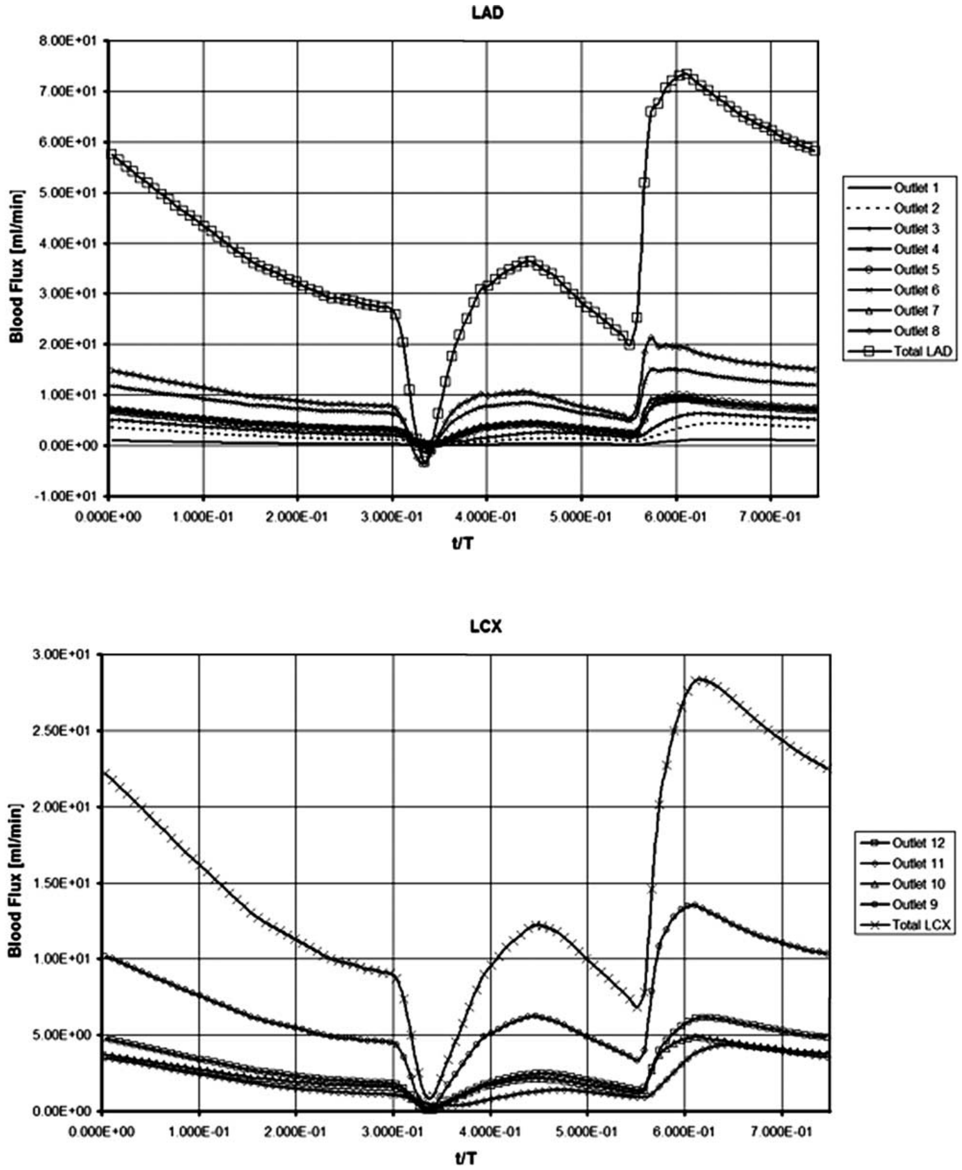


Fig. 4. Instantaneous blood flow in the LAD and the LCX.

major perfusion disturbances. A brief phase of flow reversal, imposed in early diastole, is more prominent at the outlets located near the LCA inlet, while it decreases progressively in outlets farther away. The effects of pulsatility are damped as the flow progresses farther downstream in the LCA tree till the flow eventually reaches a quasi steady capillary bed value.

### 3.2. Wall pressure drop and shear stress

Instantaneous wall static pressure drop with reference to the inlet and shear stress distributions during the phases of maximum and minimum coronary inflow are depicted in Figs. 5 and 6, respectively. The maximum wall shear stress spatial variation was calculated to be approximately 17 Pa, whereas the corresponding maximum wall pressure drop reached to 250 Pa or equivalently to 1.875 mmHg. The value of the wall pressure drop is a fair estimate of the pressure head needed to drive the flow through the various branches of the coronary tree. Evidently, as long as the blood flux between two arbitrary network points increases, so does the corresponding pressure difference. The existence of a coronary stenosis would also increase the required pressure difference for an identical amount of blood flow.

The average wall shear stress ranged from 0.01 to 1.53 Pa for minimum and maximum inflow, respectively. These values lie within the baseline value of 2 Pa suggested for most arteries in a wide range of species [2]. It can be clearly discerned (Fig. 6) that the wall surface, which surrounds the orifices of the various bifurcating arterial branches, contains regions of significant spatial shear stress variations. Similar patterns may be observed at both time instances that are depicted here. Additionally, it can be seen that the regions of high and low wall shear stress interchange during the phases

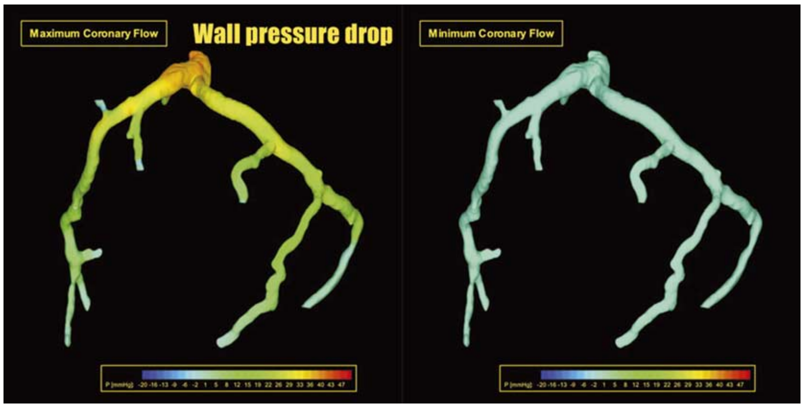


Fig. 5. Wall pressure drop: at maximum and minimum coronary flow.

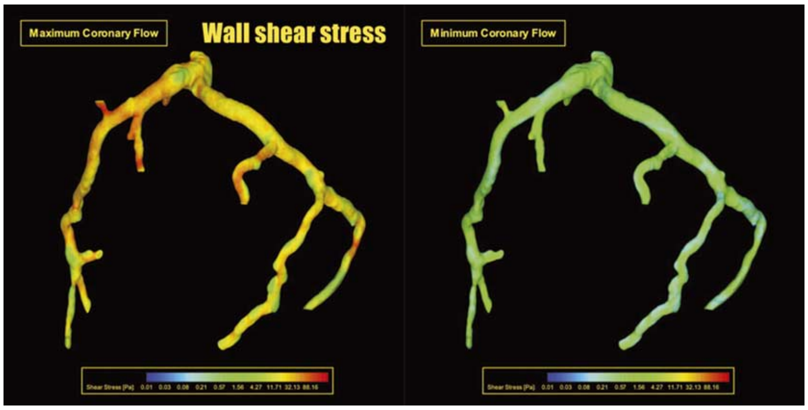


Fig. 6. Wall shear stress distribution: at maximum and minimum coronary flow.

of maximum and minimum coronary inflow, thus indicating the existence of significant temporal shear stress gradients as well. Such circumstances are considered as evidence for the existence of disturbed blood flow regions and pinpoint possible sites for atherogenesis (Video 1).

### 3.3. Velocity streamlines

A close-up view (Fig. 7) of the instantaneous velocity streamlines in the vicinity of the origin of second marginal branch of the LCX may reveal the underlying meaning of disturbed flow as discussed above. As anticipated, during the phase of maximum coronary inflow, the velocity field separates smoothly into two downstream branches. On the contrary, during the phase of minimum inflow, a rather large vortical structure is generated causing extensive recirculation at the entrance of the branch with the larger diameter. This is reflected by large spatial shear stress gradients on the vessel wall.

## 4. Discussion

This study aimed to explore the potential of computational techniques for simulating intracoronary flows. Since conventional imaging of coronary arteries on

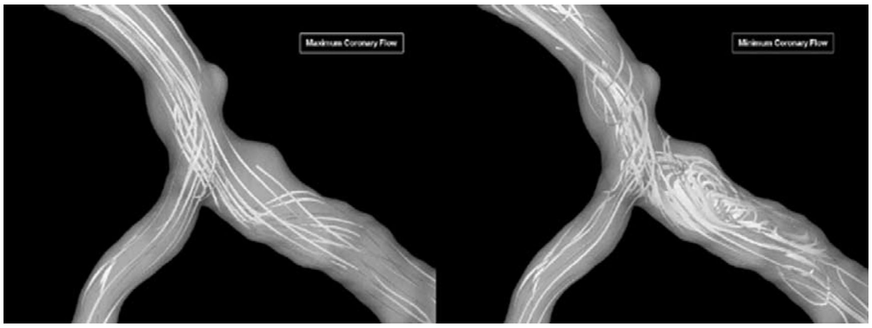

Fig. 7. Coronary flow velocity streamlines: at maximum and minimum coronary flow.

the beating heart, until recently, had been insufficient for use in computational flow simulation, this study tried to derive an anatomically accurate 3D coronary arterial tree from an explanted porcine heart by excluding coronary motion and thus avoiding the motion blur. However, it is the complexity of the coronary geometry and blood flow physiology, which makes its hemodynamic calculations extremely challenging.

Magnetic resonance (MR) [18] and intravascular ultrasound (IVUS) [19]-based techniques have been described to provide valuable diagnostic and anatomical information; however their temporal and spatial resolution is usually not sufficient for deriving information based on the differentiated velocity vector field such as the wall shear stress distribution [20]. CFD techniques, on the other hand can provide a significantly larger amount of information on coronary flow dynamics, with greater spatial and temporal resolution, non-invasively, on a patient-specific basis and within a completely virtual environment.

The basic prerequisites for computational flow simulation in a vascular system include an accurate volumetric 3D geometry, and realistic inlet plus outlet boundary flow conditions. The adoption of a generic inflow boundary condition suitably fits to the scope of this study in exploring the feasibility of intracoronary flow computations. However, use of MR-based measurements of instantaneous inflow could go a long way to generate a patient-specific flow simulation. The choice of a general type of outflow boundary conditions implies that all artificial outlets are positioned on arterial branches belonging to the same branch generation. There are several systems for classifying such tree like geometries [4]. Unfortunately, in most cases such classification is not practically feasible and great care is needed in the field of image acquisition and segmentation. There is no particular difference when substituting these with the ‘zero normal stress’ boundary condition, apart from the fact that you get an unsteady pressure outlet profile. Whatever the case, the pressure drop effectively remains unchanged. To provide realistic patient-specific flow simulations, however, some sort of outlet pressure information would be needed. The problem of acquiring accurate outlet boundary conditions on a said patient, which for the moment seems to require an invasive procedure, is yet to be solved satisfactorily.

The absence of any phase shift in the blood flux profiles as shown in Fig. 4 is of course a simplification. It only respects the incompressibility of the continuum used in the present calculations. It is the arterial wall distensibility that is expected to change the phases. Currently we are in the process of developing all the modules that are necessary for these calculations.

The complex independent motion of the coronaries as imposed by the movement of the myocardium is a parameter that will have to be incorporated, to render greater accuracy to such calculations. Experimental investigations aiming at coronary motion registration are currently under way [17]. It is our purpose to utilize such data and evaluate any additional inertial forces imposed on coronary blood flow. Most computational investigations on these inertial effects have been constrained to simplified tube-like models of the coronary geometry [7,21]. In a more recent study of the effects of realistic coronary motion upon a model of the right main coronary artery [22], it was shown that motion itself has little influence on the time averaged values of the wall shear stress, which is the most sensitive quantity of our system. On the other hand, it affects the instantaneous variations of the calculated quantities. However, this influence is significantly smaller than the effects of pulsatility when compared to an equivalent steady flow investigation [22]. Therefore, the inclusion of realistic coronary wall cyclic displacement is expected to affect the instantaneous values of the shear stress and its gradients. It is not expected to influence integrated quantities like the blood mass fluxes or time averaged values of wall and shear stress distributions. In short, the currently available scientific data suggests that the main characterizing factor of intracoronary flow is its pulsatile nature, which is incorporated in our model.

That a generic dataset of human coronary flow physiology was used in a porcine coronary geometry to develop this computational tool is a limitation of this study. However, with the availability of high resolution coronary geometries using state-of-the-art multislice CT scanners (Fig. 8), the above-developed tool is ready for adaptation and is suitable for offline computations of in vivo hearts.

In spite of various challenges, the potential ability to visualize a coronary stenosis in three dimensions, in contrast to bi-plane imaging, to calculate mass flow ratios across

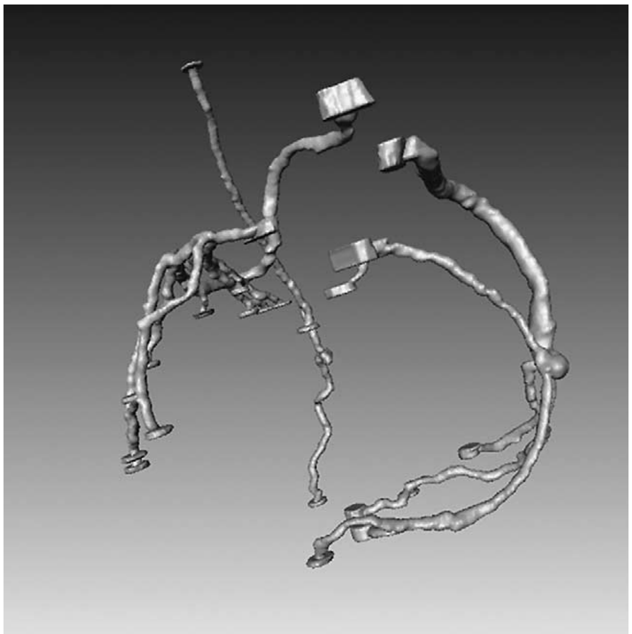

Fig. 8. Post CABG graft coronary geometry acquired using multislice CT scanner.

branches and to be able to objectively observe their influences on the distal end organ flow and pressure appears to be a very exciting concept. Multislice CT scanners providing isotropic datasets of high temporal and spatial resolution that are optimal for 3D reconstructions, have already brought into the realm of reality, the possibility of getting in vivo human coronary and bypass graft images (Fig. 8). The ability to perform such flow simulations on a patient-specific basis in a totally virtual environment, non-invasively and thus repetitively, could lend these techniques an important role as a predictive tool, which means that such simulations could predict potential flare-up scenarios where preventive measures could be instituted. Several investigations that are underway, reveal the important contributions that CFD can offer when combined with presently available diagnostic techniques [13,23,24].

The presently developed model is in the process of being adapted to simulate flow in graft to coronary geometries, e.g. end to side anastomosis. Further work would also be required on deriving patient-specific realistic boundary conditions. However, once successful this tool could assist in precise surgical/interventional planning so as to impart the most optimum flow characteristics to the graft-coronary geometry, thus improving the longevity of the graft. It could eventually become complimentary to imaging devices such as the CT scanner, so that the simulations can be performed and superimposed on a 3D image, offline or online depending on the available computing abilities. One can foresee computations being part of the imaging technology paralleling what color Doppler is to echocardiography. Once non-invasive coronary imaging matches the gold standard of cine-angiography, such applications could provide a full data set of the actual luminal volume occupied by stenosis, their effect on distal flow, their effect on exercise flow reserve and if need be repetitive non-invasive examinations to depict the progress or regression of disease. On the other hand these techniques would be very useful in optimal designing and evolution of proximal and distal graft anastomotic devices.

Hemodynamic stresses constitute one of the backbones for the development and the progression of atherosclerosis. Reliable depiction of spatial distribution of shear stress in the coronary arterial tree could provide a useful tool for studying the role of hemodynamic stresses in atherogenesis [13].

With the presently available computational capabilities, such a simulation needs days to be performed. However, with the continuous doubling of circuit density in computer chips and hence expectantly of the computing speed in almost every 2 years, (Moore's law) [25], we would hope that these computations will be performed in shorter times. If this trend in technological advancement continues for another couple of decades as expected, it will be realistic to assume that computational tools shall provide unprecedented amount of objectivity and discretization in observing biological flows. From the bioengineering point of view, the challenge is located in developing a robust tool, which could predict the adaptation of the coronary arterial system to a new pressure flow equilibrium relationship. The latter is directly the outcome of the specific anatomy/geometry of the true lumen and of any topological alterations incurred by disease or surgery.

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## Appendix A. Conference discussion

***Dr B. Walpoth*** (*Geneva, Switzerland*): Your work is a little bit futuristic, but very nice. Have you as well been looking at quantitative flow at different points? This could be done by MR. Could you comment on the issue of spatial resolution and flow quantitation.

***Dr Dave***: My slides showed that this technique precisely measures the mass/flow ratios. And the software has been validated in mechanical systems to the precision that if this coronary artery model, which is real, is actually a non-distendible tube, then this amount of flow will go through the LAD and the rest will go to the circumflex. The tool has been developed so as to work in a linear flow model; the Reynolds number used in this calculation was based assuming that the flow would be laminar. If there is a stenosis in the coronary system, then the local Reynolds numbers are likely to be very high. And then you need to supplement it with another software. But this is in the scheme of things, and with the availability of real human geometry, we are soon likely to use this tool in patient geometries. I would speculate that such a tool could have a lot of use in studying competitive flow, use of arterial grafts, use of sequential anastomosis with the vein as compared to separate vein stenosis. And furthering the domain, we could also use this to simulate the flow in 1-1/2 ventricle repair or in Fontan's circulation.

***Dr A. Wechsler*** (*Philadelphia, PA, USA*): And to resolve some of the issues related to angles of connection of various connectors and it has a lot of very practical applications.

***Dr Dave***: Absolutely. In fact, before the era of automatic anastomosis, we hardly used to think how long and what orientation of the graft would optimize the flow. However for the development of anastomotic tools, you need to define these precisely. And such tools would help go a long way in defining optimal mechanical aspects of the anastomosis, so that the driving pressure is not lost in the angulations, that the graft coronary interphase provides the linearmost flow thus probably increasing the longevity of our anastomoses.